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<120> METHODS OF TREATMENT OF TYPE 2 DIABETES

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<140> UNKNOWN

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<160> 30

<170> PatentIn Ver. 2.0

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Cys His Thr Arg Ala Leu Pro Gly Ala Trp Val Lys Gly Gln Ser Ala
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Leu Arg Val Ser Glu Pro Ser Glu Val Tyr Ile Ala Val Leu Gln Arg
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Tyr Gln Ala Val Gly Leu His Leu Trp Lys Val Glu Lys Arg Arg Val
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His Ala Tyr Asp Arg Glu Val His Leu Arg Cys Glu Leu Ser Pro Gly
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Tyr Tyr Leu Ala Val Pro Ser Thr Phe Leu Lys Asp Ala Pro Gly Glu
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Ser Tyr Glu His Leu Trp Ala Gly Gln Val Ala Asp Ala Leu Val Asp
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His Ala Tyr Asp Arg Glu Val His Leu Arg Cys Glu Leu Ser Pro Gly
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Tyr Tyr Leu Ala Val Pro Ser Thr Phe Leu Lys Asp Ala Pro Gly Glu
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 Ala Leu Gln Lys Ser Arg His Leu Leu Asp Gln Val Ile Pro Pro Gly
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 Ser Tyr Glu His Leu Trp Ala Gly Gln Val Ala Asp Ala Leu Val Asp

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Gln Pro Ser Trp Ala Asp Gln Glu Tyr Arg Gly Ser Phe Thr Cys Arg	100	105	110
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Pro Cys Leu Ala Gly Arg Leu Cys Phe Ser Arg Cys Gln Arg Glu Asp	130	135	140
Val Phe Trp Leu Pro Leu Leu Glu Lys Gly Pro Trp Val Leu Arg Ala	145	150	155
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<210> 14
 <211> 139
 <212> PRT
 <213> Human

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Pro	Leu	Ala	Gln	Phe	Arg	Glu	Asp	Ile	Thr	Trp	Arg	Arg	Pro	Gln	Glu
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Ala	Leu	Gln	Lys	Ser	Arg	His	Leu	Leu	Asp	Gln	Val	Ser	Cys	Pro	Val
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Gln	Leu	Pro	Ala	Asp	Trp	Thr	Cys	Lys	Val	Gln	Pro	Val	Trp	Leu	Glu
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Phe	Pro	Cys	Leu	Pro	Ile	Ser	Cys	Arg	Leu	Arg	Val	Ser	Ser	Asp	Thr
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 <213> Human

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 35 40 45
 Pro Glu Gly Gly Arg Ser Gln Asp Ala Pro Pro Leu Leu Leu Gln Glu
 50 55 60
 Pro Leu Leu Ser Cys Val Pro His Arg Tyr Ala Gln Glu Val Ser Arg
 65 70 75 80
 Leu Cys Leu Leu Pro Ala Gly Thr Tyr Lys Val Val Pro Ser Thr Tyr
 85 90 95
 Leu Pro Asp Thr Glu Gly Ala Phe Thr Val Thr Ile Ala Thr Arg Ile
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 Asp Arg Pro Ser Ile His Ser Gln Glu Met Leu Gly Gln Phe Leu Gln
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Glu Val Ser Val Met Ala Val Met Lys Thr
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<212> DNA
<213> Human

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<211> 666
<212> PRT
<213> Mus musculus

<400> 18
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35 40 45
Ile Cys Ala Thr Pro Gln Leu Phe Pro Asp Asn Pro Trp Glu Gly Gln
50 55 60
Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala
65 70 75 80
Ala Leu Gln Lys Ser Gln His Leu Leu Asp Gln Val Phe Pro Pro Gly
85 90 95
Gln Pro Gly Trp Ser Asp Gln Lys Tyr Gln Gly Phe Phe Thr Cys Arg
100 105 110
Ile Trp Gln Phe Gly His Trp Glu Glu Val Thr Ile Asp Asp Arg Leu
115 120 125
Pro Cys Leu Ala Gly Arg Leu Cys Phe Ser Arg Cys Gln Arg Glu Asp
130 135 140
Val Phe Trp Leu Pro Leu Leu Glu Lys Ala Tyr Ala Lys Val His Gly
145 150 155 160

Ser	Tyr	Glu	His	Leu	Trp	Ala	Gly	Gln	Val	Ala	Asp	Ala	Leu	Val	Asp	
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Leu	Thr	Gly	Ser	Leu	Ala	Glu	Arg	Trp	Ser	Leu	Lys	Asp	Val	Thr	Lys	
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Ala	Ser	Gly	Gln	Gln	Asp	Arg	Pro	Ser	Gly	Gly	Glu	His	Arg	Thr	Cys	
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Leu	Ser	Pro	Arg	Ala	Gly	Ala	Arg	Glu	Leu	Gly	Glu	Phe	His	Ala	Phe	
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Ile	Ile	Ser	Asp	Leu	Gln	Glu	Leu	Arg	Ser	Gln	Thr	Gly	Gln	Gly	Ile	
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Cys	His	Thr	Arg	Thr	Leu	Pro	Gly	Ala	Trp	Val	Thr	Gly	Gln	Ser	Ala	
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Gly	Gly	Cys	Arg	Asn	Asn	Ser	Cys	Phe	Pro	Cys	Asn	Pro	Lys	Phe	Trp	
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Pro	Arg	Arg	Arg	Leu	Val	Gly	Gln	Thr	Arg	Ala	Leu	Ala	Gly	Ala	Ser	
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Pro	Ala	Pro	Val	Asn	Leu	Pro	Gly	Lys	Asp	Tyr	Gln	Ala	Val	Gly	Leu	
				405					410					415		
His	Ile	Trp	Lys	Val	Glu	Lys	Arg	Lys	Ile	Ser	Leu	Pro	Arg	Val	Leu	
			420					425					430			
Ser	Ala	Pro	Pro	Val	Ala	Gly	Thr	Ala	Cys	His	Ala	Tyr	Asp	Arg	Glu	
		435					440					445				
Ile	His	Leu	Arg	Cys	Glu	Leu	Ser	Pro	Gly	Tyr	Tyr	Leu	Ala	Val	Pro	
	450					455					460					
Ser	Thr	Phe	Leu	Lys	Asp	Val	Pro	Gly	Gln	Phe	Leu	Leu	Arg	Val	Phe	
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Phe Thr Gly Lys Ile Ser Leu Ser Ala Val Arg Leu Ala Thr Lys Gly
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Ala Ser Pro Gly Thr Ala Leu Pro Ala Gly Glu Trp Glu Thr Val Gln
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Leu Gln Gly Cys Trp Arg Ala Gly Gln Thr Ala Gly Gly Ser Arg Asn
515 520 525

Phe Ala Ser Tyr Pro Cys Asn Pro Cys Leu Pro Phe Ser Val Pro Glu
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Gly Ala Gly Pro Arg Tyr Ile Arg Ile Thr Leu Gln Gln His Cys Arg
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Leu Ser Asp Ser Gln Leu His Pro Ile Gly Phe His Val Phe Gln Val
565 570 575

Pro Ala Asp Gly Glu Asn Gln Asp Ala Cys Ser Leu Leu Leu Gln Glu
580 585 590

Pro Leu Leu Ser Cys Val Pro His Arg Tyr Ala Gln Glu Val Ser Arg
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Leu Cys Leu Leu Ser Val Gly Asn Tyr Arg Ile Val Pro Ser Thr Tyr
610 615 620

Leu Pro Asp Thr Glu Gly Thr Phe Thr Val Thr Ile Ala Thr Arg Ile
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Asp Arg Gln Ser Ile His Ser Gln Glu Met Leu Gly Gln Leu Leu Gln
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<210> 19
<211> 2511
<212> DNA
<213> Mus musculus

<400> 19
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 <211> 309
 <212> PRT
 <213> Human

<400> 20

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			20					25					30		
Leu	Gly	Leu	Leu	Leu	Asn	Ser	Leu	Ala	Leu	Trp	Val	Phe	Cys	Cys	Arg
		35					40					45			
Met	Gln	Gln	Trp	Thr	Glu	Thr	Arg	Ile	Tyr	Met	Thr	Asn	Leu	Ala	Val
	50					55					60				
Ala	Asp	Leu	Cys	Leu	Leu	Cys	Thr	Leu	Pro	Phe	Val	Leu	His	Ser	Leu
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Arg	Asp	Thr	Ser	Asp	Thr	Pro	Leu	Cys	Gln	Leu	Ser	Gln	Gly	Ile	Tyr
				85					90					95	
Leu	Thr	Asn	Arg	Tyr	Met	Ser	Ile	Ser	Leu	Val	Thr	Ala	Ile	Ala	Val
		100						105					110		
Asp	Arg	Tyr	Val	Ala	Val	Arg	His	Pro	Leu	Arg	Ala	Arg	Gly	Leu	Arg
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Ser	Pro	Arg	Gln	Ala	Ala	Ala	Val	Cys	Ala	Val	Leu	Trp	Val	Leu	Val
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Lys Val Val Thr Ala Leu Ala Gln Arg Pro Pro Thr Asp Val Gly Gln
195 200 205

Ala Glu Ala Thr Arg Lys Ala Ala Arg Met Val Trp Ala Asn Leu Leu
210 215 220

Val Phe Val Val Cys Phe Leu Pro Leu His Val Gly Leu Thr Val Arg
225 230 235 240

Leu Ala Val Gly Trp Asn Ala Cys Ala Leu Leu Glu Thr Ile Arg Arg
245 250 255

Ala Leu Tyr Ile Thr Ser Lys Leu Ser Asp Ala Asn Cys Cys Leu Asp
260 265 270

Ala Ile Cys Tyr Tyr Tyr Met Ala Lys Glu Phe Gln Glu Ala Ser Ala
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Leu Ala Val Ala Pro Arg Ala Lys Ala His Lys Ser Gln Asp Ser Leu
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Cys Val Thr Leu Ala
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<211> 1875
<212> DNA
<213> Human

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<400> 22

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 35 40 45

Cys Leu Gln Ser Gly Thr Leu Phe Arg Asp Glu Ala Phe Pro Pro Val
 50 55 60

Pro Gln Ser Leu Gly Tyr Lys Asp Leu Gly Pro Asn Ser Ser Lys Thr
 65 70 75 80

Tyr Gly Ile Lys Trp Lys Arg Pro Thr Glu Leu Leu Ser Asn Pro Gln
 85 90 95

Phe Ile Val Asp Gly Ala Thr Arg Thr Asp Ile Cys Gln Gly Ala Leu
 100 105 110

Gly Asp Cys Trp Leu Leu Ala Ala Ile Ala Ser Leu Thr Leu Asn Asp
 115 120 125

Thr Leu Leu His Arg Val Val Pro His Gly Gln Ser Phe Gln Asn Gly
 130 135 140

Tyr Ala Gly Ile Phe His Phe Gln Leu Trp Gln Phe Gly Glu Trp Val
 145 150 155 160

Asp Val Val Val Asp Asp Leu Leu Pro Ile Lys Asp Gly Lys Leu Val
 165 170 175

Phe Val His Ser Ala Glu Gly Asn Glu Phe Trp Ser Ala Leu Leu Glu
 180 185 190

Lys Ala Tyr Ala Lys Val Asn Gly Ser Tyr Glu Ala Leu Ser Gly Gly
 195 200 205

Ser Thr Ser Glu Gly Phe Glu Asp Phe Thr Gly Gly Val Thr Glu Trp
 210 215 220

Tyr Glu Leu Arg Lys Ala Pro Ser Asp Leu Tyr Gln Ile Ile Leu Lys
 225 230 235 240

Ala Leu Glu Arg Gly Ser Leu Leu Gly Cys Ser Ile Asp Ile Ser Ser

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Ala	Tyr	Ser	Val	Thr	Gly	Ala	Lys	Gln	Val	Asn	Tyr	Arg	Gly	Gln	Val				
		275					280					285							
Val	Ser	Leu	Ile	Arg	Met	Arg	Asn	Pro	Trp	Gly	Glu	Val	Glu	Trp	Thr				
	290					295				300									
Gly	Ala	Trp	Ser	Asp	Ser	Ser	Ser	Glu	Trp	Asn	Asn	Val	Asp	Pro	Tyr				
305					310					315					320				
Glu	Arg	Asp	Gln	Leu	Arg	Val	Lys	Met	Glu	Asp	Gly	Glu	Phe	Trp	Met				
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Ser	Phe	Arg	Asp	Phe	Met	Arg	Glu	Phe	Thr	Arg	Leu	Glu	Ile	Cys	Asn				
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Leu	Thr	Pro	Asp	Ala	Leu	Lys	Ser	Arg	Thr	Ile	Arg	Lys	Trp	Asn	Thr				
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Thr	Leu	Tyr	Glu	Gly	Thr	Trp	Arg	Arg	Gly	Ser	Thr	Ala	Gly	Gly	Cys				
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Cys	Ser	Phe	Val	Leu	Ala	Leu	Met	Gln	Lys	His	Arg	Arg	Arg	Glu	Arg				
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Arg	Phe	Gly	Arg	Asp	Met	Glu	Thr	Ile	Gly	Phe	Ala	Val	Tyr	Glu	Val				
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Pro	Pro	Glu	Leu	Val	Gly	Gln	Pro	Ala	Val	His	Leu	Lys	Arg	Asp	Phe				
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Phe	Leu	Ala	Asn	Ala	Ser	Arg	Ala	Arg	Ser	Glu	Gln	Phe	Ile	Asn	Leu				
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Val	Pro	Ser	Thr	Phe	Glu	Pro	Asn	Lys	Glu	Gly	Asp	Phe	Val	Leu	Arg				
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Gln	Ala	Asn	Leu	Pro	Asp	Glu	Gln	Val	Leu	Ser	Glu	Glu	Glu	Ile	Asp				
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Glu	Asn	Phe	Lys	Ala	Leu	Phe	Arg	Gln	Leu	Ala	Gly	Glu	Asp	Met	Glu				
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Ile	Ser	Val	Lys	Glu	Leu	Arg	Thr	Ile	Leu	Asn	Arg	Ile	Ile	Ser	Lys				
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His	Lys	Asp	Leu	Arg	Thr	Lys	Gly	Phe	Ser	Leu	Glu	Ser	Cys	Arg	Ser	580	585	590
Met	Val	Asn	Leu	Met	Asp	Arg	Asp	Gly	Asn	Gly	Lys	Leu	Gly	Leu	Val	595	600	605
Glu	Phe	Asn	Ile	Leu	Trp	Asn	Arg	Ile	Arg	Asn	Tyr	Leu	Ser	Ile	Phe	610	615	620
Arg	Lys	Phe	Asp	Leu	Asp	Lys	Ser	Gly	Ser	Met	Ser	Ala	Tyr	Glu	Met	625	630	635
Arg	Met	Ala	Ile	Glu	Ser	Ala	Gly	Phe	Lys	Leu	Asn	Lys	Lys	Leu	Tyr	645	650	655
Glu	Leu	Ile	Ile	Thr	Arg	Tyr	Ser	Glu	Pro	Asp	Leu	Ala	Val	Asp	Phe	660	665	670
Asp	Asn	Phe	Val	Cys	Cys	Leu	Val	Arg	Leu	Glu	Thr	Met	Phe	Arg	Phe	675	680	685
Phe	Lys	Thr	Leu	Asp	Thr	Asp	Leu	Asp	Gly	Val	Val	Thr	Phe	Asp	Leu	690	695	700
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Glu	Ala	Leu	Arg	Asn	Glu	Cys	Leu	Glu	Ala	Gly	Thr	Leu	Phe	Gln	Asp	35	40	45
Pro	Ser	Phe	Pro	Ala	Ile	Pro	Ser	Ala	Leu	Gly	Phe	Lys	Glu	Leu	Gly	50	55	60
Pro	Tyr	Ser	Ser	Lys	Thr	Arg	Gly	Met	Arg	Trp	Lys	Arg	Pro	Thr	Glu	65	70	75
Ile	Cys	Ala	Asp	Pro	Gln	Phe	Ile	Ile	Gly	Gly	Ala	Thr	Arg	Thr	Asp	85	90	95
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Ser	Leu	Thr	Leu	Asn	Glu	Glu	Ile	Leu	Ala	Arg	Val	Val	Pro	Leu	Asn	115	120	125
Gln	Ser	Phe	Gln	Glu	Asn	Tyr	Ala	Gly	Ile	Phe	His	Phe	Gln	Phe	Trp	130	135	140

Gln	Tyr	Gly	Glu	Trp	Val	Glu	Val	Val	Val	Asp	Asp	Arg	Leu	Pro	Thr	
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Lys	Asp	Gly	Glu	Leu	Leu	Phe	Val	His	Ser	Ala	Glu	Gly	Ser	Glu	Phe	
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Trp	Ser	Ala	Leu	Leu	Glu	Lys	Ala	Tyr	Ala	Lys	Ile	Asn	Gly	Cys	Tyr	
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Arg	Leu	Glu	Ile	Cys	Asn	Leu	Thr	Pro	Asp	Thr	Leu	Thr	Ser	Asp	Thr	
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Tyr	Lys	Lys	Trp	Lys	Leu	Thr	Lys	Met	Asp	Gly	Asn	Trp	Arg	Arg	Gly	
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Gly	Glu	Ser	Gly	Cys	Thr	Phe	Leu	Val	Gly	Leu	Ile	Gln	Lys	His	Arg	
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Arg	Arg	Gln	Arg	Lys	Met	Gly	Glu	Asp	Met	His	Thr	Ile	Gly	Phe	Gly	
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Ile	Tyr	Glu	Val	Pro	Glu	Glu	Leu	Ser	Gly	Gln	Thr	Asn	Ile	His	Leu	
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06701

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Glu  Ala  Gly  Gly  Gly  Asn  Pro  Ser  Gly  Ile  Tyr  Ser  Ala  Ile  Ile  Ser
          35          40          45

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Pro	Pro	Asp	Glu	Thr	Ser	Leu	Phe	Tyr	Ser	Gln	Lys	Phe	Pro	Ile	Gln	
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Phe	Val	Trp	Lys	Arg	Pro	Pro	Glu	Ile	Cys	Glu	Asn	Pro	Arg	Phe	Ile	
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Ile	Asp	Gly	Ala	Asn	Arg	Thr	Asp	Ile	Cys	Gln	Gly	Glu	Leu	Gly	Asp	
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Cys	Trp	Phe	Leu	Ala	Ala	Ile	Ala	Cys	Leu	Thr	Leu	Asn	Gln	His	Leu	
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Leu	Phe	Arg	Val	Ile	Pro	His	Asp	Gln	Ser	Phe	Ile	Glu	Asn	Tyr	Ala	
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Gly	Ile	Phe	His	Phe	Gln	Phe	Trp	Arg	Tyr	Gly	Glu	Trp	Val	Asp	Val	
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Val	Ile	Asp	Asp	Cys	Leu	Pro	Thr	Tyr	Asn	Asn	Gln	Leu	Val	Phe	Thr	
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Lys	Ser	Asn	His	Arg	Asn	Glu	Phe	Trp	Ser	Ala	Leu	Leu	Glu	Lys	Ala	
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Tyr	Ala	Lys	Leu	His	Gly	Ser	Tyr	Glu	Ala	Leu	Lys	Gly	Gly	Asn	Thr	
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Thr	Tyr	Gly	Thr	Ser	Pro	Ser	Gly	Leu	Asn	Met	Gly	Glu	Leu	Ile	Ala	
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Gln	Tyr	Glu	Thr	Arg	Met	Ala	Cys	Gly	Leu	Val	Arg	Gly	His	Ala	Tyr	
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Leu	Val	Arg	Leu	Arg	Asn	Pro	Trp	Gly	Gln	Val	Glu	Trp	Asn	Gly	Ser	
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Trp	Ser	Asp	Arg	Trp	Lys	Asp	Trp	Ser	Phe	Val	Asp	Lys	Asp	Glu	Lys	

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Tyr Glu Asp Phe Ile Tyr His Phe Thr Lys Leu Glu Ile Cys Asn Leu				
	405		410	415
Thr Ala Asp Ala Leu Gln Ser Asp Lys Leu Gln Thr Trp Thr Val Ser				
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Val Asn Glu Gly Arg Trp Val Arg Gly Cys Ser Ala Gly Gly Cys Arg				
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Asn Phe Pro Asp Thr Phe Trp Thr Asn Pro Gln Tyr Arg Leu Lys Leu				
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Leu Glu Glu Asp Asp Asp Pro Asp Asp Ser Glu Val Ile Cys Ser Phe				
	465		470	475 480
Leu Val Ala Leu Met Gln Lys Asn Arg Arg Lys Asp Arg Lys Leu Gly				
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Ala Ser Leu Phe Thr Ile Gly Phe Ala Ile Tyr Glu Val Pro Lys Glu				
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Met His Gly Asn Lys Gln His Leu Gln Lys Asp Phe Phe Leu Tyr Asn				
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Ala Ser Lys Ala Arg Ser Lys Thr Tyr Ile Asn Met Arg Glu Val Ser				
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Gln Arg Phe Arg Leu Pro Pro Ser Glu Tyr Val Ile Val Pro Ser Thr				
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Tyr Glu Pro His Gln Glu Gly Glu Phe Ile Leu Arg Val Phe Ser Glu				
	565		570	575
Lys Arg Asn Leu Ser Glu Glu Val Glu Asn Thr Ile Ser Val Asp Arg				
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Pro Val Lys Lys Lys Lys Thr Lys Pro Ile Ile Phe Val Ser Asp Arg				
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Ala Asn Ser Asn Lys Glu Leu Gly Val Asp Gln Glu Ser Glu Glu Gly				
	610		615	620
Lys Gly Lys Thr Ser Pro Asp Lys Gln Lys Gln Ser Pro Gln Pro Gln				
	625		630	635 640
Pro Gly Ser Ser Asp Gln Glu Ser Glu Glu Gln Gln Gln Phe Arg Asn				
	645		650	655
Ile Phe Lys Gln Ile Ala Gly Asp Asp Met Glu Ile Cys Ala Asp Glu				
	660		665	670
Leu Lys Lys Val Leu Asn Thr Val Val Asn Lys His Lys Asp Leu Lys				
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Thr His Gly Phe Thr Leu Glu Ser Cys Arg Ser Met Ile Ala Leu Met				
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Asp Thr Asp Gly Ser Gly Lys Leu Asn Leu Gln Glu Phe His His Leu
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 Trp Asn Lys Ile Lys Ala Trp Gln Lys Ile Phe Lys His Tyr Asp Thr
 725 730 735
 Asp Gln Ser Gly Thr Ile Asn Ser Tyr Glu Met Arg Asn Ala Val Asn
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 Asp Ala Gly Phe His Leu Asn Asn Gln Leu Tyr Asp Ile Ile Thr Met
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 Arg Tyr Ala Asp Lys His Met Asn Ile Asp Phe Asp Ser Phe Ile Cys
 770 775 780
 Cys Phe Val Arg Leu Glu Gly Met Phe Arg Ala Phe His Ala Phe Asp
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 Val Arg Arg Lys Arg Pro Lys Gly Ile Cys Glu Asp Pro Arg Leu Phe
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 Val Asp Gly Ile Ser Ser His Asp Leu His Gln Gly Gln Val Gly Asn
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 Cys Trp Phe Val Ala Ala Cys Ser Ser Leu Ala Ser Arg Glu Ser Leu
 85 90 95
 Trp Gln Lys Val Ile Pro Asp Trp Lys Glu Gln Glu Trp Asp Pro Glu
 100 105 110
 Lys Pro Asn Ala Tyr Ala Gly Ile Phe His Phe His Phe Trp Arg Phe
 115 120 125
 Gly Trp Val Asp Val Val Ile Asp Asp Arg Leu Pro Thr Val Asn Asn
 130 135 140
 Gln Leu Ile Tyr Cys His Ser Asn Ser Arg Asn Glu Phe Trp Cys Ala
 145 150 155 160

Leu Val Glu Lys Ala Tyr Ala Lys Leu Ala Gly Cys Tyr Gln Ala Leu
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 Asp Gly Gly Asn Thr Ala Asp Ala Leu Val Asp Phe Thr Gly Gly Val
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 Ser Glu Pro Ile Asp Leu Thr Glu Gly Asp Phe Ala Asn Asp Glu Thr
 195 200 205
 Lys Arg Asn Gln Leu Phe Glu Arg Met Leu Lys Val His Ser Arg Gly
 210 215 220
 Gly Leu Ile Ser Ala Ser Ile Lys Ala Val Thr Ala Ala Asp Met Glu
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 Ala Arg Leu Ala Cys Gly Leu Val Lys Gly His Ala Tyr Ala Val Thr
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 Asp Val Arg Lys Val Arg Leu Gly His Gly Leu Leu Ala Phe Phe Lys
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 Ile Tyr Ile Asn Ser Arg Ser Val Phe Leu Arg Thr Asp Gln Pro Glu
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 Gly Arg Tyr Val Ile Ile Pro Thr Thr Phe Glu Pro Gly His Thr Gly
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515 520 525

Lys Asp Ser Pro Thr Gly Ala Asn Ser Tyr Val Ile Ile Lys Cys Glu
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Gly Asp Lys Val Arg Ser Ala Val Gln Lys Gly Thr Ser Thr Pro Glu
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Tyr Asn Val Lys Gly Ile Phe Tyr Arg Lys Lys Leu Ser Gln Pro Ile
565 570 575

Thr Val Gln Val Trp Asn His Arg Val Leu Lys Asp Glu Phe Leu Gly
580 585 590

Gln Val His Leu Lys Ala Asp Pro Asp Asn Leu Gln Ala Leu His Thr
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35 40 45

Val Val Trp Lys Arg Pro Gln Asp Ile Ser Asp Asp Pro His Leu Ile
50 55 60

Val Gly Asn Ile Ser Asn His Gln Leu Ile Gln Gly Arg Leu Gly Asn
65 70 75 80

Lys Ala Met Ile Ser Ala Phe Ser Cys Leu Ala Val Gln Glu Ser His
85 90 95

Trp Thr Lys Ala Ile Pro Asn His Lys Asp Gln Glu Trp Asp Pro Arg
100 105 110

Lys Pro Glu Lys Tyr Ala Gly Ile Phe His Phe Arg Phe Trp His Phe
115 120 125

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Glu Phe Leu Leu Arg	Ile Phe Ser Glu Val	Pro Val Gln Leu Arg Glu		
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Tyr Pro Lys Val Val	Thr Gln Ile Thr Val	His Ser Ala Glu Gly Leu		
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Cys Gly Lys Glu Glu	Val Arg Ser Pro Val	Gln Lys Asn Thr Val His		
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	595	600	605	
Lys Ser Leu Tyr Leu	Arg Lys Lys Gly Gly	Pro Thr Ala Lys Val Lys		
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TD4T3D 4899450

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Gln	Ser	Phe	Gln	Lys	Asp	Tyr	Ala	Gly	Ile	Phe	His	Phe	Gln	Phe	Trp				
	130					135					140								
Gln	Tyr	Gly	Glu	Trp	Val	Glu	Val	Val	Ile	Asp	Asp	Arg	Leu	Pro	Thr				
145					150					155					160				
Lys	Asn	Gly	Gln	Leu	Leu	Phe	Leu	His	Ser	Glu	Glu	Gly	Asn	Glu	Phe				
				165					170					175					
Trp	Ser	Ala	Leu	Leu	Glu	Lys	Ala	Tyr	Ala	Lys	Leu	Asn	Gly	Ser	Tyr				
			180					185					190						
Glu	Ala	Leu	Val	Gly	Gly	Ser	Thr	Ile	Glu	Gly	Phe	Glu	Asp	Phe	Thr				
			195				200					205							
Gly	Gly	Ile	Ser	Glu	Phe	Tyr	Asp	Leu	Lys	Lys	Pro	Pro	Glu	Asn	Leu				
	210					215					220								
Tyr	Tyr	Ile	Ile	Gln	Lys	Ala	Leu	Arg	Lys	Gly	Ser	Leu	Leu	Gly	Cys				
225					230					235					240				
Ser	Ile	Asp	Val	Ser	Thr	Ala	Ala	Glu	Ala	Glu	Ala	Thr	Thr	Arg	Gln				
				245					250					255					
Lys	Leu	Val	Lys	Gly	His	Ala	Tyr	Ser	Val	Thr	Gly	Val	Glu	Glu	Val				
			260					265					270						
Asn	Phe	His	Gly	Arg	Pro	Glu	Lys	Leu	Ile	Arg	Leu	Arg	Asn	Pro	Trp				
		275					280					285							
Gly	Glu	Val	Glu	Trp	Ser	Gly	Ala	Trp	Ser	Asp	Asn	Ala	Pro	Glu	Trp				
	290					295					300								
Asn	Tyr	Ile	Asp	Pro	Arg	Arg	Lys	Glu	Glu	Leu	Asp	Lys	Lys	Ala	Glu				
305					310					315					320				
Asp	Gly	Glu	Phe	Trp	Met	Ser	Phe	Ser	Asp	Phe	Leu	Lys	Gln	Tyr	Ser				
				325					330					335					
Arg	Leu	Glu	Ile	Cys	Asn	Leu	Ser	Pro	Asp	Ser	Leu	Ser	Ser	Glu	Glu				
			340					345					350						
Ile	His	Lys	Trp	Asn	Leu	Val	Leu	Phe	Asn	Gly	Arg	Trp	Thr	Arg	Gly				
		355					360				365								
Ser	Thr	Ala	Gly	Gly	Cys	Leu	Asn	Tyr	Pro	Gly	Thr	Tyr	Trp	Thr	Asn				
	370					375					380								
Pro	Gln	Phe	Lys	Ile	His	Leu	Asp	Glu	Val	Asp	Glu	Asp	Gln	Glu	Glu				
385					390					395					400				
Gly	Thr	Ser	Glu	Pro	Cys	Cys	Thr	Val	Leu	Leu	Gly	Leu	Met	Gln	Lys				
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Asn	Arg	Arg	Arg	Gln	Lys	Arg	Ile	Gly	Gln	Gly	Met	Leu	Ser	Ile	Gly
			420					425					430		
Tyr	Ala	Val	Tyr	Gln	Ile	Pro	Lys	Glu	Leu	Glu	Ser	His	Thr	Asp	Ala
		435					440					445			
His	Leu	Gly	Arg	Asp	Phe	Phe	Leu	Gly	Arg	Gln	Pro	Ser	Thr	Cys	Ser
	450					455					460				
Ser	Thr	Tyr	Met	Asn	Leu	Arg	Glu	Val	Ser	Ser	Arg	Val	Arg	Leu	Pro
465					470					475					480
Pro	Gly	Gln	Tyr	Leu	Val	Val	Pro	Ser	Thr	Phe	Glu	Pro	Phe	Lys	Asp
				485					490					495	
Gly	Asp	Phe	Cys	Leu	Arg	Val	Phe	Ser	Glu	Lys	Lys	Ala	Lys	Ala	Leu
			500					505					510		
Glu	Ile	Gly	Asp	Thr	Val	Ser	Gly	His	Pro	His	Glu	Pro	His	Pro	Arg
		515					520					525			
Asp	Met	Asp	Glu	Glu	Asp	Glu	His	Val	Arg	Ser	Leu	Phe	Glu	Glu	Phe
	530					535					540				
Val	Gly	Lys	Asp	Ser	Glu	Ile	Ser	Ala	Asn	Gln	Leu	Lys	Arg	Val	Leu
545					550				555						560
Asn	Glu	Val	Leu	Ser	Lys	Arg	Thr	Asp	Met	Lys	Phe	Asp	Gly	Phe	Asn
				565					570					575	
Ile	Asn	Thr	Cys	Arg	Glu	Met	Ile	Ser	Leu	Leu	Asp	Ser	Asp	Gly	Thr
			580					585					590		
Gly	Ser	Leu	Gly	Pro	Met	Glu	Phe	Lys	Thr	Leu	Trp	Leu	Lys	Ile	Arg
		595					600					605			
Thr	Tyr	Leu	Glu	Ile	Phe	Gln	Glu	Met	Asp	His	Asn	His	Val	Gly	Thr
	610					615					620				
Ile	Glu	Ala	His	Glu	Met	Arg	Thr	Ala	Leu	Lys	Lys	Ala	Gly	Phe	Thr
625					630					635					640
Leu	Asn	Asn	Gln	Val	Gln	Gln	Thr	Ile	Ala	Met	Arg	Tyr	Ala	Cys	Ser
				645					650					655	
Lys	Leu	Gly	Val	Asp	Phe	Asn	Gly	Phe	Val	Ala	Cys	Met	Ile	Arg	Leu
			660					665					670		
Glu	Thr	Leu	Phe	Lys	Leu	Phe	Arg	Leu	Leu	Asp	Lys	Asp	Gln	Asn	Gly
		675					680					685			
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<400> 28

Met	Pro	Tyr	Leu	Tyr	Arg	Ala	Pro	Gly	Pro	Gln	Ala	His	Pro	Val	Pro	1	5	10	15
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Arg	Gln	Glu	Cys	Leu	Gln	Arg	Gly	Thr	Leu	Phe	Glu	Asp	Ala	Asp	Phe	35	40	45	
Pro	Ala	Ser	Asn	Ser	Ser	Leu	Phe	Tyr	Ser	Glu	Arg	Pro	Gln	Ile	Pro	50	55	60	
Phe	Val	Trp	Lys	Arg	Pro	Gly	Glu	Ile	Val	Lys	Asn	Pro	Glu	Phe	Ile	65	70	75	80
Leu	Gly	Gly	Ala	Thr	Arg	Thr	Asp	Ile	Cys	Gln	Gly	Glu	Leu	Gly	Asp	85	90	95	
Cys	Trp	Leu	Leu	Ala	Ala	Ile	Ala	Ser	Leu	Thr	Leu	Asn	Gln	Lys	Ala	100	105	110	
Leu	Ala	Arg	Val	Ile	Pro	Gln	Asp	Gln	Ser	Phe	Gly	Pro	Gly	Tyr	Ala	115	120	125	
Gly	Ile	Phe	His	Phe	Gln	Phe	Trp	Gln	His	Ser	Glu	Trp	Leu	Asp	Val	130	135	140	
Val	Ile	Asp	Asp	Arg	Leu	Pro	Thr	Phe	Arg	Asp	Arg	Leu	Val	Phe	Leu	145	150	155	160
His	Ser	Ala	Asp	His	Asn	Glu	Phe	Trp	Ser	Ala	Leu	Leu	Glu	Lys	Ala	165	170	175	
Tyr	Ala	Lys	Leu	Asn	Gly	Ser	Tyr	Glu	Ala	Leu	Lys	Gly	Gly	Ser	Ala	180	185	190	
Ile	Glu	Ala	Met	Glu	Asp	Phe	Thr	Gly	Gly	Val	Ala	Glu	Thr	Phe	Gln	195	200	205	
Thr	Lys	Glu	Ala	Pro	Glu	Asn	Phe	Tyr	Glu	Ile	Leu	Glu	Lys	Ala	Leu	210	215	220	
Lys	Arg	Gly	Ser	Leu	Leu	Gly	Cys	Phe	Ile	Asp	Thr	Arg	Ser	Ala	Ala	225	230	235	240
Glu	Ser	Glu	Ala	Arg	Thr	Pro	Phe	Gly	Leu	Ile	Lys	Gly	His	Ala	Tyr	245	250	255	
Ser	Val	Thr	Gly	Ile	Asp	Gln	Val	Ser	Phe	Arg	Gly	Gln	Arg	Ile	Glu	260	265	270	
Leu	Ile	Arg	Ile	Arg	Asn	Pro	Trp	Gly	Gln	Val	Glu	Trp	Asn	Gly	Ser	275	280	285	
Trp	Ser	Asp	Ser	Ser	Pro	Glu	Trp	Arg	Ser	Val	Gly	Pro	Ala	Glu	Gln	290	295	300	
Lys	Arg	Leu	Cys	His	Thr	Ala	Leu	Asp	Asp	Gly	Glu	Phe	Trp	Met	Ala	305	310	315	320

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Phe Lys Asp Phe Lys Ala His Phe Asp Lys Val Glu Ile Cys Asn Leu
325 330 335

Thr Pro Asp Ala Leu Glu Glu Asp Ala Ile His Lys Trp Glu Val Thr
340 345 350

Val His Gln Gly Ser Trp Val Arg Gly Ser Thr Ala Gly Gly Cys Arg
355 360 365

Asn Phe Leu Asp Thr Phe Trp Thr Asn Pro Gln Ile Lys Leu Ser Leu
370 375 380

Thr Glu Lys Asp Glu Gly Gln Glu Glu Cys Ser Phe Leu Val Ala Leu
385 390 395 400

Met Gln Lys Asp Arg Arg Lys Leu Lys Arg Phe Gly Ala Asn Val Leu
405 410 415

Thr Ile Gly Tyr Ala Ile Tyr Glu Cys Pro Asp Lys Asp Glu His Leu
420 425 430

Asn Lys Asp Phe Phe Arg Tyr His Ala Ser Arg Ala Arg Ser Lys Thr
435 440 445

Phe Ile Asn Leu Arg Glu Val Ser Asp Arg Phe Lys Leu Pro Pro Gly
450 455 460

Glu Tyr Ile Leu Ile Pro Ser Thr Phe Glu Pro His Gln Glu Ala Asp
465 470 475 480

Phe Cys Leu Arg Ile Phe Ser Glu Lys Lys Ala Ile Thr Arg Asp Met
485 490 495

Asp Gly Asn Val Asp Ile Asp Leu Pro Glu Pro Pro Lys Pro Thr Pro
500 505 510

Pro Asp Gln Glu Thr Glu Glu Glu Gln Arg Phe Arg Ala Leu Phe Glu
515 520 525

Gln Val Ala Gly Glu Asp Met Glu Val Thr Ala Glu Glu Leu Glu Tyr
530 535 540

Val Leu Asn Ala Val Leu Gln Lys Lys Lys Asp Ile Lys Phe Lys Lys
545 550 555 560

Leu Ser Leu Ile Ser Cys Lys Asn Ile Ile Ser Leu Met Asp Thr Ser
565 570 575

Gly Asn Gly Lys Leu Glu Phe Asp Glu Phe Lys Val Phe Trp Asp Lys
580 585 590

Leu Lys Gln Trp Ile Asn Leu Phe Leu Arg Phe Asp Ala Asp Lys Ser
595 600 605

Gly Thr Met Ser Thr Tyr Glu Leu Arg Thr Ala Leu Lys Ala Ala Gly
610 615 620

Phe Gln Leu Ser Ser His Leu Leu Gln Leu Ile Val Leu Arg Tyr Ala
625 630 635 640

Asp Glu Glu Leu Gln Leu Asp Phe Asp Asp Phe Leu Asn Cys Leu Val

645

650

655

Arg Leu Glu Asn Ala Ser Arg Val Phe Gln Ala Leu Ser Thr Lys Asn
 660 665 670

Lys Glu Phe Ile His Leu Asn Ile Asn Glu Phe Ile His Leu Thr Met
 675 680 685

Asn Ile
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 Primer

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29

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6

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